

**REMARKS**

Applicant respectfully requests reconsideration.

Claims 1-10, 13-18, 27, 34, 42, 49, 53, 63, 69-71, 73, 84, 90, 96, 97, 107 and 116 were previously pending in this application, with claims 1-10, 13-18, 27, 34, 42, 49, 53, 73, 84, 90, 96, 97, 107 and 116 being withdrawn from consideration. Claims 2-9, 13-18, 27, and 96-97 have been cancelled without prejudice or disclaimer. Applicant reserves the right to pursue these and other claims in continuation applications.

Claims 63 and 71 have been amended. Support for the amendments is found at least on page 4, lines 1-5, page 6, lines 19-21, page 22, lines 8-10, page 33, lines 3-6 and lines 15-21, page 34, lines 26-29 and page 36, lines 25-28.

New claims 134-140 have been added. Support for these claims is found throughout the application, specifically at least on page 3, lines 16-19, page 4, lines 1-6 and page 6, lines 12-14, and in the claims as originally filed (see claims 64-68, and 72). No new matter has been added.

As a result, claims 63, 69-71, and 134-140 are pending for examination with claims 63 and 71 being independent claims.

No new matter has been added.

**Election/Restriction**

Applicant acknowledges that the Examiner has made the Restriction Requirement final. Claims 1-10, 13-18, 27, 34, 42, 49, 53, 73, 84, 90, 96, 97, 107 and 116 are withdrawn from further consideration. Applicant reiterates herewith the request for rejoinder of claims upon the allowance of the product claims according to MPEP § 821.04, as indicated in the Restriction Requirement of October 13, 2006. Rejoinder is requested for claims 1, 10, 34, 42, 49, 53, 73, 84, 90, 107, and 116. Upon indication from the Examiner that such claims would be rejoined, Applicant would amend the currently withdrawn claims to recite all limitations of or to depend from the product claims currently under examination.

### Objections to the Specification

The Examiner has objected to the title of the invention and has requested a new title indicative of the invention to which the claims are directed. Applicant presents a replacement title and requests reconsideration.

### Rejections under 35 U.S.C. § 112

Claims 63 and 69-71 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Applicant has amended the claims to address each of the issues raised by the Examiner. Claim 63 has been amended to recite "An isolated nucleic acid molecule, comprising (a) a nucleic acid molecule...". Claims 63 and 71 have been amended to clarify that the production of a polysaccharide is enhanced relative to the level produced from a wild-type bacterium. Claims 63 and 71 have been amended to recite "enhances production of a polysaccharide from a coding region of an *ica* locus when operably linked to an *ica* nucleic acid". Claim 71 has been amended to recite that the fragment spans nucleotides 23 and 24 of SEQ ID NO.:1. Support for the amendments is found at least on page 4, lines 1-5, page 6, lines 19-21, page 22, lines 8-10, page 33, lines 3-6 and lines 15-21, page 34, lines 26-29 and page 36, lines 25-28.

Reconsideration and withdrawal of this objection is respectfully requested.

Claims 63 and 69-71 are rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the enablement requirement as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention.

Applicant respectfully traverses in part. Claims 63 and 71 have been amended to clarify the claim language. The amended claims are adequately disclosed in the specification to enable one of ordinary skill in the art to practice the invention. The test of enablement is whether undue or unreasonable experimentation is required for one of ordinary skill in the art to make and use the claimed invention. The factors to be considered in determining whether undue experimentation is required include 1) the nature of the invention; 2) the breadth of the claims; 3)

the state of the art; 4) the level of ordinary skill in the art; 5) the level of predictability in the art; 6) the amount of direction provided by the inventor(s); 7) the existence of working examples; and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731; 8 USPQ 2d 1400 (Fed. Cir. 1988). These factors are to be considered in their totality with no one factor being dispositive of the issue of enablement. The Examiner has cited the Wands factors but has not performed a complete Wands analysis to establish a prima facie case of lack of enablement. Applicant asserts that a complete analysis of the Wands factors, as presented below, does not support the Examiner's assertion that the claims are not enabled.

#### The Nature of the Invention

The nature of the invention is the discovery that a mutation within nucleotides 23 and 29 of wildtype nucleic acid sequence SEQ ID NO.:2 can lead to the over-production of polysaccharide, and fragments that span nucleotides 23 and 24 of mutant nucleic acid sequence SEQ ID NO.:1 can lead to the over-production of polysaccharide.

#### The Breadth of the Claims

Applicant asserts that the claims are not overly broad. Applicant has claimed nucleic acid molecules that hybridize to specific nucleic acid sequences that are disclosed in the application. The invention relates to isolated nucleic acid molecules that hybridize to a nucleic acid molecule having a sequence of SEQ ID NO.:2, where the nucleic acid molecule spans nucleotides 23 and 29 of SEQ ID NO.:2 and has an addition, deletion or substitution of at least two nucleotides and that enhances the production of a polysaccharide. The invention also relates to isolated nucleic acid molecules that are fragments of a nucleic acid molecule having a sequence of SEQ ID NO.:1 where the fragment spans nucleotides 23 and 24 of SEQ ID NO.:1 and enhances the production of a polysaccharide.

#### The State of the Prior Art

Applicant has discovered that a mutation in the *ica* locus results in increased production of bacterial polysaccharide. The production of bacterial polysaccharides was known to those of

ordinary skill in the art at the time of filing the application. Applicant discloses that the production of the polysaccharide is dependent upon the proteins encoded by the intracellular adhesion (*ica*) locus which has been reported to be present in both *S. epidermidis* and *S. aureus* (Cramton *et al.*, 1999; Helimann *et al.*, 1996; McKenney *et al.*, 1998, previously cited, see page 16, line 32 to page 17, line 2). The five genes that make up the *ica* locus and the nucleic acid sequences are known to those of ordinary skill in the art and disclosed in the application on page 17, lines 3-4. Applicant has provided hybridization conditions to allow one of ordinary skill in the art to detect the nucleic acid molecules of the invention. The art was familiar with methods for hybridization of nucleic acid molecules at the time of filing the application.

#### The Level of Ordinary Skill in the Art

The level of skill would be that of a microbiologist with a Bachelor's degree and such a person would know how to practice the invention using experimental procedures that would be considered routine.

#### The Level of Predictability in the Art

Applicant asserts that the art is predictable relating to detecting nucleic acid molecules that hybridize to a known nucleic acid sequence using disclosed hybridization conditions. The nucleic acid sequences of both wildtype and mutant have been provided. Applicant has disclosed the structural and functional limitations of the claimed compositions including the nucleic acid sequence (SEQ ID NO.:2) to which the nucleic acid molecules of the invention hybridize as well as specific hybridization conditions. Applicant has also disclosed a mutant sequence (SEQ ID NO.:1) from which fragments that span nucleotides 23 and 24 of this sequence can be made.

#### The Amount of Direction in the Specification

Adequate guidance has been provided in the specification to allow one of ordinary skill in the art to make and use the claimed invention. The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). According to the MPEP § 2164.03, “[t]he amount of guidance or direction” refers to that

information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification.” Applicant asserts that one of ordinary skill in the art would know how to make and use the claimed nucleic acid molecules and fragments based on the teaching in the application and the knowledge in the art.

Applicant has disclosed that a mutation of this region of SEQ ID NO.:2 spanning nucleotides 24 and 28, results in enhanced production of polysaccharide. The application discloses that a nucleic acid comprising a mutation (i.e. addition, deletion or substitution) in the 5 nucleotide motif may be used to enhance polysaccharide production from a bacterium (see page 20, lines 16-17). The specification provides nucleotide sequences with and without mutations (SEQ ID NO.:1 (mutant nucleic acid sequence) and SEQ ID NO.:2 (wildtype nucleic acid sequence)), the specific location of the mutation required to enhance the production of polysaccharide (page 4, lines 1-3), and methods for detecting such nucleic acid molecules and fragments (see page 8, line 4 to page 9, line 3) and enhanced polysaccharide production (see page 40, lines 19-26). One of ordinary skill in the art would be able to make nucleic acids that hybridize to SEQ ID NO.:2 and fragments of SEQ ID NO.:1, and be able to determine if such fragments are capable of enhancing the production of polysaccharide using no more than routine experimentation. Applicant has therefore provided adequate guidance to one of ordinary skill in the art to enable them to make and use the claimed nucleic acid molecules of the invention.

Applicant respectfully traverses the Examiner’s statement that “applicants have not sufficiently defined the conditions under which the hybridizations are to take place” (see Office Action, pages 4-5). Applicant has disclosed on page 33, lines 15-29 hybridization conditions contemplated by the invention as stringent conditions. One of ordinary skill in the art would be able to determine nucleic acid molecules that hybridize to SEQ ID NO.:2 using the disclosed conditions. However, in the interest of expediting prosecution, Applicant has amended claim 63 to recite the disclosed hybridization conditions. The Examiner has indicated on pages 4-5 of the Office Action that such recitation would aid in overcoming this portion of the rejection.

### The Presence or Absence of Working Examples

With respect to the working examples, the court in *In re Wright* stated that “Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples.” *In re Wright* 999 F.2d 1557, 1561, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993) citing *In re Marzocchi* 439 F.2d 220, 223, 169 USPQ 367, 369 (C.C.P.A. 1971). Applicant has described and claimed the invention in a manner that is readily understandable to one of ordinary skill in the art, and has also provided illustrative working examples. The Examples demonstrate that a five nucleotide deletion within the specified region of the disclosed nucleic acid sequence results in enhanced polysaccharide production compared with the polysaccharide production from a wildtype. For example, Example 1, pages 41-50, demonstrates that *S. aureus* MN8m having a mutation in the region that includes nucleotide residues 24 and 28 of SEQ ID NO.:2 is an overproducer of polysaccharide (i.e. enhances production of polysaccharide) compared to wildtype. This example further demonstrates that making mutations in this region of the wildtype *S. aureus* MN8 resulted in an overproducer of polysaccharide.

### The Quantity of Experimentation

Applicant asserts that there is no undue experimentation required for one of ordinary skill in the art to practice the invention as claimed. Mutations of nucleic acid sequences involving additions, deletions or substitutions are within the scope of those of ordinary skill in the art and would not require guidance outside of Applicant’s disclosure. One of ordinary skill in the art need only make at least two additions, deletions or mutations within the specific disclosed nucleic acid region, perform a routine hybridization assay to detect binding of the nucleic acid molecule and perform the methods disclosed in the application to detect enhanced polysaccharide production as explained *supra* in order to practice the claimed invention. With respect to fragments as in claim 71, one of ordinary skill in the art is provided the nucleic acid sequence of mutant SEQ ID NO.:1 and need only make a fragment that spans nucleotides 23 and 24 of this nucleic acid sequence and perform the methods disclosed in the application to detect enhanced polysaccharide production. No undue experimentation is required.

Applicant maintains that full consideration of each and all of the *Wands* factors leads one to the reasonable conclusion that practicing the invention would not require undue experimentation.

Reconsideration and withdrawal of this rejection is respectfully requested.

Claims 63 and 69-71 are rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Applicant had possession of the claimed invention at the time the application was filed.

Applicant respectfully traverses in part. As described above, the amended claims are adequately disclosed in the specification and the claims have been amended to clarify the claimed invention. The specific nucleic acid sequences of SEQ ID NO.:2 (wildtype) and SEQ ID NO.:1 (mutant) are disclosed. Applicant has provided examples that demonstrate differences in polysaccharide production using these nucleic acid sequences.

A representative number of species is deemed to be disclosed when the disclosed species are representative of the entire genus (see MPEP § 2163 at page 2100-176). According to the MPEP § 2163:

“[w]hat constitutes a “representative number” is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a “representative number” depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed.”

The nucleic acid sequences of the claimed invention are structurally similar – the only difference between SEQ ID NO.:1 and SEQ ID NO.:2 is a five nucleotide deletion in a specific region of the nucleic acid sequence. Applicant has specified that it is this region of SEQ ID NO.:2 where mutations (i.e. addition, deletion or substitution) can be made to produce a nucleic acid molecule of the invention. The structure-function relationship of the nucleic acid molecules of the claimed invention is such that the nucleic acid molecule spans a specified region of either SEQ ID NO.:2 (nucleotides 23-29) or SEQ ID NO.:1 (nucleotides 23 and 24) and that the nucleic

acid molecule enhances the production of polysaccharide relative to the level produced from a wildtype bacterium.

Therefore, Applicant has disclosed sequences encompassed by the claimed invention, disclosed the specific region that mutations can occur to result in a nucleic acid molecule or fragment of the invention, and has provided examples demonstrating that such sequences result in enhanced production of polysaccharide. Applicant asserts that they fully possessed the claimed invention at the time the application was filed.

Reconsideration and withdrawal of this objection is respectfully requested.

Rejections Under 35 U.S.C. § 102

Claims 63, 69 and 70 are rejected under 35 U.S.C. § 102(b) as being anticipated by Pier *et al.* (Accession AAZ87998, May 31, 2000) and PCT Publication No. WO 00/03745.

Applicant respectfully traverses in part. Claim 63 has been amended to recite a nucleic acid molecule that has an addition, deletion or substitution of at least two nucleotides in a region between and including nucleotides 24 and 28 of SEQ ID NO.:2. The sequence of Pier *et al.* as aligned by the Examiner with SEQ ID NO.:2, shows only a single nucleotide substitution in this region. Therefore, Pier *et al.* does not teach each and every limitation of the claims and does not anticipate the claimed invention.

Reconsideration and withdrawal of this objection is respectfully requested.



Claim 71 is rejected under 35 U.S.C. § 102(b) as being anticipated by Cramton *et al.* (Accession AF086783, October 1, 1999).

Applicant respectfully traverses. Claim 71 as amended recites that the fragment spans a region of SEQ ID NO.:1 having a five nucleotide deletion between and including nucleotides 24 and 28 of SEQ ID NO.:2. The sequence identified by the Examiner in Cramton *et al.* and aligned with SEQ ID NO.:1 is a wildtype sequence and therefore includes this five nucleotide region (i.e., TATTT). The claimed invention however covers nucleic acids that span and yet are mutant in this region. Therefore, Cramton *et al.* does not teach each and every limitation of the claims and does not anticipate the claimed invention.

Reconsideration and withdrawal of this objection is respectfully requested.

**CONCLUSION**

Applicant respectfully requests reconsideration. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. A check in the amount of \$1,020.00 is enclosed herewith to cover the three month extension of time. If there is a further fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,



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